

- c. an expression of the corresponding mRNA in primary cells of the thymus, fetal liver, adult spleen, or bone marrow;
- d. is encoded by a cDNA comprising repeat sequences of SEQ ID NOS: 6 and 7;
- e. wherein the corresponding mRNA comprises mRNA species of differing length, said mRNA species comprising:
  - i. identical 3' regions corresponding to the coding region of SEQ ID NO:2; and
  - ii. non-identical 5' regions.

37. (Thrice Amended) Protein according to claim 36, wherein said protein comprises at least one of the following features:

- a. said protein is encoded by a corresponding mRNA which shows an *in vitro* upregulation and/or accumulation if a three day allogeneic spleen cell reaction is carried out with non-irradiated, not pretreated spleen cells of mouse strains CBA and C57B1/6;
- b. having AT rich regions in the cDNA, the 3' part of which encodes the protein; or
- c. inducible by a serum factor present in fetal calf serum.

38. (Twice Amended) Protein according to claim 36, wherein one or more of SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, or of repeat sequences hybridizing to SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, or SEQ ID NO:10 under stringent conditions are present in the DNA encoding the protein, said stringent conditions comprising hybridization at 65°C in an aqueous solution.

41. (Thrice Amended) Protein according to claim 36, wherein said protein comprises a partial amino acid sequence encoded by a DNA hybridizing to a fragment of the cDNA or SEQ ID NO:1 or NO:2 or NO:4 under stringent conditions, wherein said fragment retains said differentiation-inducing activity.

42. (Twice Amended) Protein according to claim 36, comprising variants of said protein comprising an amino acid sequence wherein said variant retains said differentiation inducing activity on friend erythroleukemia cell line or a fusion protein comprising said protein of Claim 36 or said variant.

62. (Twice Amended) A therapeutic composition comprising:

- a. the protein of Claim 36, or a variant or fragment of said protein wherein said variant or fragment retains said differentiation-inducing activity; and
- b. a conventional carrier and/or excipient in an amount effective to treat diseases accompanied by impairment of differentiation inducing activity in erythropoietic cells.

72. (Four Times Amended) An isolated protein with differentiation-inducing activity on Friend erythroleukemia cell lines comprising the following properties:

- a. induction of differentiation in Friend erythroleukemia cell lines with hemoglobin formation;
- b. a molecular weight in the range of about 10-60 kDa as determined by gel filtration on a cross-linked allyl dextran;
- c. expression of the corresponding mRNA in primary cells of the thymus, fetal liver, adult spleen, or bone marrow;
- d. is encoded by a cDNA comprising repeat sequences of SEQ ID NOS: 6 and 7 or sequences which hybridize with said repeat sequences under stringent conditions;
- e. wherein the corresponding mRNA comprises mRNA species of differing length, said mRNA species comprising:
  - i. identical 3' regions corresponding to the coding region of SEQ ID NO:2 or sequences which hybridize with said coding region under stringent conditions; and
  - ii. non-identical 5' regions,

wherein said stringent conditions comprise hybridization at 65°C in an aqueous solution or at 42°C in 50% formamide and subsequent washing of the filter at 60°C in an aqueous solution having a salt concentration of 15mM NaCl and a concentration of SDS of 0.1%.

#### **REMARKS**

The Applicant wishes to thank the Examiner again for the productive interview on July 8, 2002. During the interview it was discussed how the current 35 U.S.C. § 112, first paragraph rejection regarding variants and fragments could be overcome. Additionally, the 35 U.S.C. § 102(b) rejection over the Dormer et al. reference was discussed regarding the appropriateness